MICRO CASE 15 --- M. tb (post primary tb)

A 32 year old Hispanic woman presented with a **cough** for several weeks and a 15-lb **weight lo**ss. She also had night sweats and subjective fevers and felt fatigued. Despite erythromycin treatment for suspected pneumonia, her fever and cough progressively got worse. She complained about **coughing blood-tinged sputum.**

She had **emigrated from Venezuela** to the U.S. three years before her illness, but she frequently returned to Venezuela to visit relatives.

* Physical Examination
  + Bilateral rales and lymphadenopathy
* Imaging
  + Right upper lobe infiltrate
* DIAGNOSTIC WORK UP
  + Skin test
  + Gram and acid fast stain of respiratory secretions
  + Cultures of respiratory secretions
  + Broth and agar-based mycobacterial cultures and DNA probe-based identification
  + In failed Gram and acid fast stain, fungal serology and fungal cultures
* DIFFERENTIAL DIAGNOSIS
  + Actinomyces, Anaerobes (aspiration pneumonia), Endemic fungi (e.g. Histoplasma capsulatum), Legionella penumophila, Mycoplasma pneumonia, Nocardia sp
  + Immigrants from endemic country\*\*
* MICROBIOLOGICAL PROPERTIES
  + Acid fast bacteria (reactive to auramine O fluorescence and Kinyoun acid fast stains)
  + Cell wall contains 60% lipids in long-chain fatty acids (=mycolic acids)
  + Grows slowly on selective (e.g. Lowenstein-Jensen agar) media
  + \*\***Virulent strain grow in parallel and serpentine pattern due to presence of cord factor (6,6 trehalose-dimycolate), a virulence factor**
  + **\*\*Phenolic glycolipids (e.g. LAM) contribute to enhanced virulence**
  + Mycobacteria are resistant to acid and alkali and dehydration
* EPIDEMIOLOGY
  + Exposure to airborne organisms from a symptomatic patient is the major mode of contagion (people with pulmonary tb produce respiratory aerosol)
  + Risk is highest among children less than 3 years old, lowest in later childhood, and high again among adolescents, young adults and very old and immunocompromised individuals.
  + \*\*Risk is DIRECTLY related to DEGREE of exposure and not related to genetic and other host factors.
* PATHOGENESIS
  + Major determinants of type and extent of disease = patients age, immune status, and the mycobacterial load
  + Obligate aerobes and therefore cause disease only in highly oxygenated tissues, such as upper lobe of lung
  + Facultative intracellular bacteria 🡪 Hide within macrophages. LAM is recognized by macrophage mannose receptor. M. tb also expresses a C4 convertase, forming C3b on its surface which can then be bound by CR4 of macrophage, causing M. tb to be taken up by macrophage.
  + M.tb evades phagocytic killing by inhibiting phagolysosome fusion. This is mediated by a tryptophan-aspartate containing coat protein on bacteria
  + Mycobacterial glycolipid antigens on MHC II do NOT produce a RAPID immune response
  + Bacteria proliferate in phagosome, eventually bursting macrophages and infecting neighbor macrophages
  + **Cord factor** is toxic to PMNs and also stimulates formation of granulomas. **TB granulomas may be visualized by chest XR as lobar (Ghon focus) or perihilar lymph node involvement, reflecting primary infection.**
  + Elicits CD4+ and CD8+ T cells. TH1 cells release **IFN gamma** to stimulate macrophage activation. TH1 cells also release IL-12, TNF and **NO** (NO is the key molecule for M tb killing)
  + 90% of tb infections are latent (bacterial replication within granulomas balanced with killing)
  + **Reactivation (aka post-primary infectio**n) can occur from age, illness, etc. Material within granuloma becomes caseous. Central area of granuloma undergoes necrosis and may break into bronchi, discharging M. tb into air via cough. Phagocytes also cause considerable tissue damage.
* TREATMENT
  + Involves multiple drugs and long term treatment
  + RIPE: Rifampin, Isoniazid, Pyrazinamide, and Ethambutol
  + Use drug susceptibility test to determine drug usage
    - For susceptible isolate, RIF and INH usually used
    - For unsusceptible isolates (multidrug restistant Tb meaning resistant to INH and RIF at least) usually involves 4-5 drugs: ciprofloxacin, amikacin, ethionamide, and cycloserine
  + HIV patients infected with non-tb mycobacteria receive a macrolide, rifabutin, and other drugs
* PREVENTION
  + In super-endemic areas, given **BCG vaccine**. Vaccine can protect against meningitis
  + **INH therapy** in **exposed individuals** (with positive PPD) younger than 35 (tho children cannot be placed on INH)